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GENERATION OF XENOGENEIC ANTIBODIES

ABSTRACT OF THE DISCLOSURE

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The subject invention provides non-human
mammalian hosts characterized by inactivated
endogenous Ig loci and functional human Ig loci for
response to an immunogen to produce human antibodies
10 or analogs thereof. The hosts are produced by
multiple genetic modifications of embryonic cells in
conjunction with breeding. Different strategies are
employed for recombination of the human loci randomly
or at analogous host loci. Chimeric and transgenic
15 mammals, particularly mice, are provided, having
stably integrated large, xenogeneic DNA segments. The
segments are introduced by fusion with yeast
spheroplasts comprising yeast artificial chromosomes
(YACs) which include the xenogeneic DNA segments and a
20 selective marker such as HPRT, and embryonic stem
cells.